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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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|---|---|---|
| NEWS 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS 2 | JUL 28 | CA/CAplus patent coverage enhanced |
| NEWS 3 | JUL 28 | EPFULL enhanced with additional legal status information from the epoline Register |
| NEWS 4 | JUL 28 | IFICDB, IFIPAT, and IFIUDB reloaded with enhancements |
| NEWS 5 | JUL 28 | STN Viewer performance improved |
| NEWS 6 | AUG 01 | INPADOCDB and INPAFAMDB coverage enhanced |
| NEWS 7 | AUG 13 | CA/CAplus enhanced with printed Chemical Abstracts page images from 1967-1998 |
| NEWS 8 | AUG 15 | CAOLD to be discontinued on December 31, 2008 |
| NEWS 9 | AUG 15 | CAplus currency for Korean patents enhanced |
| NEWS 10 | AUG 27 | CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information |
| NEWS 11 | SEP 18 | Support for STN Express, Versions 6.01 and earlier, to be discontinued |
| NEWS 12 | SEP 25 | CA/CAplus current-awareness alert options enhanced to accommodate supplemental CAS indexing of exemplified prophetic substances |
| NEWS 13 | SEP 26 | WPIDS, WPINDEX, and WPIX coverage of Chinese and and Korean patents enhanced |
| NEWS 14 | SEP 29 | IFICLS enhanced with new super search field |
| NEWS 15 | SEP 29 | EMBASE and EMBAL enhanced with new search and display fields |
| NEWS 16 | SEP 30 | CAS patent coverage enhanced to include exemplified prophetic substances identified in new Japanese-language patents |
| NEWS 17 | OCT 07 | EPFULL enhanced with full implementation of EPC2000 |
| NEWS 18 | OCT 07 | Multiple databases enhanced for more flexible patent number searching |
| NEWS 19 | OCT 22 | Current-awareness alert (SDI) setup and editing enhanced |
| NEWS 20 | OCT 22 | WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications |
| NEWS 21 | OCT 24 | CHEMLIST enhanced with intermediate list of pre-registered REACH substances |

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 10:51:13 ON 11 NOV 2008

=> File .Gerry2MBCE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 10:51:33 ON 11 NOV 2008

FILE 'BIOSIS' ENTERED AT 10:51:33 ON 11 NOV 2008


FILE 'CAPLUS' ENTERED AT 10:51:33 ON 11 NOV 2008


FILE 'EMBASE' ENTERED AT 10:51:33 ON 11 NOV 2008


=> S (Wallach OR Varfolomeev OR  Pewzner-Jung OR Kang OR Moshe) AND (caspase 8) (P)
hematopoiesis
L1            0 (WALLACH OR VARFOLOMEEV OR PEWZNER-JUNG OR KANG OR MOSHE) AND
                (CASPASE 8) (P) HEMATOPOIESIS

=> S (caspase 8) (P) hematopoiesis AND pd<=20041026
   1 FILES SEARCHED...
L2            3 (CASPASE 8) (P) HEMATOPOIESIS AND PD<=20041026

=> Dup Rem L2 1-3
'1-3' IS NOT VALID.  VALID FILE NAMES ARE 'BIOSIS'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> Dup Rem L2
PROCESSING COMPLETED FOR L2
L3             3 DUP REM L2 (0 DUPLICATES REMOVED)
                 ANSWERS '1-3' FROM FILE BIOSIS

=> D ibib abs L3 1-3

L3   ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
ACCESSION NUMBER:   2004:140605  BIOSIS
DOCUMENT NUMBER:    PREV200400133791
TITLE:              Simultaneous inhibition of PI3K and JAK signaling promotes
                    apoptosis in a stromal cell dependent model of B-lineage
                    acute leukemia.
AUTHOR(S):          Bertrand, Fred E. [Reprint Author]; Spengeman, Justin D.
                    [Reprint Author]; Shelton, John G. [Reprint Author];
                    McCubrey, James A. [Reprint Author]
CORPORATE SOURCE:   Department of Microbiology and Immunology, Brody School of

Medicine, East Carolina University, Greenville, NC, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 355a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 10 Mar 2004
AB Normal B-cell development depends upon interactions with the bone marrow microenvironment. This complex mixture of growth factors, extracellular matrix and stromal cells provides extrinsic signals that regulate the growth, differentiation and survival of B-cell precursors. Recent studies have demonstrated that the presence of stromal cells is capable of protecting B-lineage leukemic blasts from cytarabine and etoposide induced apoptosis in a VCAM-1 dependent mechanism. However, the precise role of the bone marrow microenvironment in the promotion of leukemic cell proliferation and apoptotic protection is not fully characterized. In normal hematopoiesis, MAP kinase signaling (p38MAPK, JNK, Raf/MEK/ERK) can be activated by a variety of cytokine stimuli and other microenvironmental cues. Similarly, the PI3K/Akt and JAK/STAT pathways can be activated by interactions with stromal cell derived factors. These signals play a role in regulating cell cycle progression and apoptosis either alone or in concert with MAP kinases. In this study we have made use of an established model system for studying interactions between B-cell precursor ALL and stromal cells, to investigate the role of MAP kinase, P3K/Akt and JAK/STAT pathways in the promotion of leukemic cell growth and survival via stromal cell contact. BLIN-2 is a pre-B ALL cell line that requires viable bone marrow stromal cell or skin fibroblast cell contact for optimal growth and survival (Shah, et al Blood 92:3817,1998; Shah et al Cancer Res 57:2268,2001). BLIN-2 cells cultured in optimum conditions (medium+stromal cells) were treated individually or in combination with small molecular weight inhibitors of JAK, MEK, PI3K, Akt, or p38MAPK and analyzed for the onset of apoptosis, DNA synthesis and caspase activation. Treatment of BLIN-2 cells with individual inhibitors did not have an effect on BLIN-2 growth much greater than that of stromal cell deprivation. Treatment of BLIN-2 cells with P3K+JAK, PI3K+MEK, or MEK+JAK inhibitor combinations resulted in an inhibition of proliferation as measured by DNA synthesis. However, only the PI3K+JAK inhibitor combination resulted in a dramatic increase in the number of annexinV+, PI+ apoptotic events. Interestingly, treatment with PI3K+JAK inhibitors did not activate caspase-3, while treatment with inhibitor combinations of PI3K+MEK and MEK+JAK did. Each of these conditions exhibited activated caspase-8; Inclusion of p38MAPK inhibitor had little effect on BLIN-2 growth and survival. Western blot analysis of activated Akt and ERK confirmed the activity of inhibitor treatments. Activated and total FKHR protein was examined in order to verify results examining Akt and PI3K inhibition. Unexpectedly, total FKHR protein was not detected in BLIN-2 cells treated individually with inhibitors of PI3K, Akt or JAK, implying the existence of a novel mechanism for FKHR regulation in BLIN-2 cells. Our data suggest that stromal cells constitutively activate the Raf/MEK/ERK, PI3K/Akt and JAK/STAT pathways to promote BLIN-2 growth and survival, but that p38MAPK is not involved. These data also indicate that two of the three activated pathways must be inactivated for efficient inhibition of BLIN-2 growth, suggesting the existence of synergy between Raf/MEK/ERK, PI3K/Akt and JAK/STAT pathways in the context of stromal cell derived anti-apoptotic signals. Identification of how these pathways interact to promote leukemic cell growth and prevent apoptosis may provide

novel theraputic targets in the treatment of ALL.

L3 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:367693 BIOSIS
DOCUMENT NUMBER: PREV200300367693
TITLE: Suppressed PP2A Activity in Fanconi Anemia C Null Cells May Allow Cell Survival Despite Constitutive Activation of PKR.
AUTHOR(S): Ruvolo, Peter P. [Reprint Author]; Suck, Garnet [Reprint Author]; Johnson, Charlene R. [Reprint Author]; Jarvis, W. David [Reprint Author]
CORPORATE SOURCE: Institute of Molecular Medicine, University of Texas Health Science Center, Houston, TX, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 4209. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 18 Sep 2003

AB Fanconi anemia is an autosomal recessive disorder that results in progressive bone marrow failure. Patients suffering from this disease show a higher incidence of acute myelocytic leukemia and other cancers compared to the rest of the population. There are at least 8 genetic complementation groups for Fanconi anemia (designated Fanc A through Fanc G). The function of the Fanc C gene product is currently not known, however, studies using knockout mice demonstrate that the Fanc C gene has a role in hematopoiesis. Cells derived from Fanc C knockout (k/o) mice and patients of the Fanc C complementation group are hypersensitive to interferon. Recent data demonstrate that the interferon-inducible kinase, PKR, is constitutively active in Fanc C k/o cells (Pang et al Blood 2001; 97: 1644). PKR is best known for its role in the inhibition of protein synthesis by phosphorylating eIF2 alpha in response to doublestranded RNA generated during viral infection or, at the cellular level, during stress stimuli. Other PKR targets have emerged including a PP2A regulatory subunit (Xu and Williams Mol. Cell Bio. 2000; 20: 5285). Since PKR has the potential to regulate PP2A, we examined PP2A activity in mouse embryonic fibroblasts (MEF) from normal and Fanc C k/o mice. Fanc C k/o MEF cells displayed 2-3 fold lower PP2A activity in both mitochondrial and nuclear membrane fractions compared to normal MEF cells even though expression of the catalytic C subunit of PP2A was higher in the Fanc C k/o cells. Lower PP2A activity in cellular compartments involved in apoptosis in Fanc C k/o MEF cells might explain how these cells might survive in spite of constitutive PKR activity. PP2A is active in intrinsic apoptotic pathways by inactivating survival molecules such as PKC alpha, Akt, and Bcl2. It is possible that suppressed PP2A activity in Fanc C k/o cells would support survival signaling cascades that would promote cell survival (e.g. reduced inhibition of PKC alpha) . Indeed, we have found that PKC alpha levels are higher in the normal MEF cells compared to Fanc C MEF cells. Furthermore, suppressed PP2A activity at the mitochondria could result in dysregulation of the intrinsic apoptotic machinery by inhibiting the inactivation of the anti-apoptotic function of Bcl2. Such a mechanism would be consistent with the recent finding that caspase 8, a component of the extrinsic apoptotic pathway, is involved in interferon-induced apoptosis in Fanconi Anemia C hematopoietic cells (Rathbun et al Blood 2000; 96: 4204).

L3 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:250087 BIOSIS
DOCUMENT NUMBER: PREV200200250087
TITLE: Evidence for a role of mitochondrial signaling in apoptosis in low-risk myelodysplastic syndromes (RA and RARS).
AUTHOR(S): Tehranchi, Ramin [Reprint author]; Fadeel, Bengt; Forsblom, Anna-Maria [Reprint author]; Christensson, Birger; Zhivotovsky, Boris; Hellstrom-Lindberg, Eva [Reprint author]
CORPORATE SOURCE: Medicine, Huddinge Hospital, Karolinska Institutet, Stockholm, Sweden
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 730a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002
AB Increased bone marrow apoptosis is considered to be the main cause of cytopenia in low-risk myelodysplastic syndromes (MDS). Indeed, several studies have demonstrated enhanced caspase activation in myelodysplastic bone marrow precursors. However, it remains to be determined whether these events are mediated via Fas/Fas-L interaction or via intrinsic activation of mitochondria. We have previously shown that blockade of Fas-R does not inhibit apoptosis or improve erythropoiesis in refractory anemia with ringed sideroblast (RARS). We also found that G-CSF reduces Fas-induced caspase-3-like activity in this FAB group, in line with the effective promotion of erythropoiesis in vivo by this cytokine. In the present study, we investigated the mitochondrial pathway for activation of caspase-3 via caspase-9 in spontaneous and Fas-induced apoptosis in patients with refractory anemia (RA) and RARS, as well as in normal bone marrow (NBM). We studied mononuclear bone marrow cells from 7 RA, 7 RARS and 9 NBM were incubated with agonistic Fas antibody in the presence or absence of z-LEHD-fmk, a caspase-9-selective inhibitor. Activation of caspase-3-like, -8 and -9 was measured repeatedly during 18 hours of culture by fluorometric enzyme assays and proliferation was investigated by 3H-Thymidine incorporation at various time points. In addition, CD34+ cells were investigated during maturation towards the GPA+ level. Base-line caspase-9 activity was significantly higher in MDS than NBM (in which it was almost absent), as was caspase-3-like and caspase-8 activity. Fas-induced caspase activity was significantly higher in MDS, with no difference between RA and RARS. The caspase-9 inhibitor effectively reduced both base-line and Fas-induced caspase-3-like activity in RA and RARS, but not in NBM. However, z-LEHD-fmk had no effect on caspase-8 activity, supporting the hypothesis that increased Fas signaling is not a major cause of apoptosis in MDS. Furthermore, caspase-9 inhibition significantly increased proliferation in both RA and RARS, whereas an inhibitory effect was seen in NBM. Cultured CD34+ cells from MDS patients showed an increased propensity for apoptosis when compared to NBM. z-LEHD-fmk increased erythroid colony growth in selected cases. Taken together, hyperactivation of the mitochondria-caspase-9 pathway is seen in low-risk MDS and appears to be more important for the induction of apoptosis than the death receptor-caspase-8 pathway. Moreover, caspase-9 inhibition in MDS was more effective in preventing Fas-induced and spontaneous apoptosis as well as in stimulating proliferation, as compared to blockade of the Fas signaling pathway or treatment of cells with caspase-3 inhibitors. On the other hand, no such effect was observed in NBM. Our data support the view that mitochondria play an important role in the ineffective

hematopoiesis in low-risk MDS.

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STN INTERNATIONAL SESSION SUSPENDED AT 10:56:05 ON 11 NOV 2008

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AT 11:55:50 ON 11 NOV 2008
FILE 'MEDLINE' ENTERED AT 11:55:50 ON 11 NOV 2008
FILE 'BIOSIS' ENTERED AT 11:55:50 ON 11 NOV 2008
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| FULL ESTIMATED COST | 39.88 | 40.09 |

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 10:51:33 ON 11 NOV 2008
L1 0 S (WALLACH OR VARFOLOMEEV OR PEWZNER-JUNG OR KANG OR MOSHE) AN
L2 3 S (CASPASE 8) (P) HEMATOPOIESIS AND PD<=20041026
L3 3 DUP REM L2 (0 DUPLICATES REMOVED)

=> S (CASPASE 8) (S) (Splice variant) AND PD<=20041026
1 FILES SEARCHED...
L4 15 (CASPASE 8) (S) (SPLICE VARIANT) AND PD<=20041026

=> Dup Rem L4
PROCESSING COMPLETED FOR L4
L5 6 DUP REM L4 (9 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE MEDLINE
ANSWERS '4-6' FROM FILE CAPLUS

=> D Ibib Abs L5 1-6

L5 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004402832 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15208670
TITLE: IG20 (MADD splice variant-5), a proapoptotic protein, interacts with DR4/DR5 and enhances TRAIL-induced apoptosis by increasing recruitment of FADD and caspase-8 to the DISC.
AUTHOR: Ramaswamy Madhu; Efimova Elena V; Martinez Osvaldo; Mulherkar Nirupama U; Singh Surya P; Prabhakar Bellur S

CORPORATE SOURCE: Department of Microbiology and Immunology, University of Illinois at Chicago, 835 South Wolcott Avenue, Chicago, IL 60612, USA.
SOURCE: Oncogene, (2004 Aug 12) Vol. 23, No. 36, pp. 6083-94.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 13 Aug 2004
Last Updated on STN: 26 Mar 2005
Entered Medline: 25 Mar 2005

AB Recently, we identified Insulinoma-Glucagonoma clone 20 (IG20) that can render cells more susceptible to tumor necrosis factor-alpha (TNF-alpha)-induced apoptosis. In addition, it can slow cell proliferation, and enhance drug- and radiation-induced cell death. TNF-related apoptosis-inducing ligand (TRAIL) can selectively induce apoptosis in some cancer cells and render others susceptible to cotreatment with drugs and irradiation, with little or no effect on most normal cells. In this study, we investigated the potential of IG20 to enhance TRAIL-induced apoptosis and found that it can render cells more susceptible to TRAIL treatment through enhanced activation of caspases. Further, we showed that this effect can be suppressed by caspase inhibitors, p35 and CrmA, and a dominant-negative Fas-associated death domain-containing protein (DN-FADD). Results from colocalization and immunoprecipitation studies showed that IG20 can interact with TRAIL death receptors (DR), DR4 and DR5 and increase recruitment of FADD and caspase-8 into the TRAIL death-inducing signaling complex (DISC). These results indicate that IG20 is a novel protein that can enhance TRAIL-induced apoptosis by facilitating DISC formation.

L5 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001316496 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11279218
TITLE: Cellular FLICE-inhibitory protein splice variants inhibit different steps of caspase -8 activation at the CD95 death-inducing signaling complex.
AUTHOR: Krueger A; Schmitz I; Baumann S; Krammer P H; Kirchhoff S
CORPORATE SOURCE: Tumor Immunology Program, German Cancer Research Center, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany.
SOURCE: The Journal of biological chemistry, (2001 Jun 8) Vol. 276, No. 23, pp. 20633-40. Electronic Publication: 2001-03-05.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 16 Jul 2001
Last Updated on STN: 5 Jan 2003
Entered Medline: 12 Jul 2001

AB Upon stimulation, CD95 (APO-1/Fas) recruits the adapter molecule FADD/MORT1, procaspase-8, and the cellular FLICE-inhibitory proteins (c-FLIP) into the death-inducing signaling complex (DISC). According to the induced proximity model, procaspase-8 is activated in the DISC in an autoproteolytic manner by two subsequent cleavage steps. c-FLIP proteins exist as a long (c-FLIP(L)) and a short (c-FLIP(S)) splice variant, both

of them capable of protecting cells from death receptor-mediated apoptosis. In stably transfected BJAB cells, both c-FLIP(S) and c-FLIP(L) block procaspase-8 activation at the DISC. However, cleavage is blocked at different steps. c-FLIP(L) allows the first cleavage step of procaspase-8, leading to the generation of the p10 subunit. In contrast, c-FLIP(S) completely inhibits cleavage of procaspase-8. Interestingly, p43-c-FLIP(L) lacking the p12 subunit also prevents cleavage of procaspase-8. In contrast, a nonprocessable mutant of c-FLIP(L) allows the first cleavage of procaspase-8. In conclusion, both c-FLIP proteins prevent caspase-8 activation at different levels of procaspase-8 processing at the DISC. Our results indicate that c-FLIP(L) induces a conformation of procaspase-8 that allows partial but not complete proteolytical processing, whereas in contrast c-FLIP(S) even prevents partial procaspase-8 activation at the DISC.

L5 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2000318377 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10860845
TITLE: Dominant expression of a novel splice variant of caspase-8 in human peripheral blood lymphocytes.
AUTHOR: Horiuchi T; Himeji D; Tsukamoto H; Harashima S; Hashimura C; Hayashi K
CORPORATE SOURCE: Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan.. horiuchi@intmed1.med.kyushu-u.ac.jp
SOURCE: Biochemical and biophysical research communications, (2000 Jun 16) Vol. 272, No. 3, pp. 877-81. Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 10 Aug 2000
Last Updated on STN: 10 Aug 2000
Entered Medline: 26 Jul 2000
AB Caspase-8 is an apical and critical proteolytic enzyme in the cascade of apoptosis. As a result of alternative splicing, the generation of at least 7 isoforms of caspase-8 has been reported. The existence of multiple isoforms that lack the essential domains for apoptosis suggests the possible role of these isoforms on the regulation of apoptosis. Here we report a novel longer isoform of caspase-8 (caspase-8L) that was generated by alternative splicing of intron 8, thereby carrying a 136-bp insertion and frame shift of the transcript. The transcript encoded N-terminal two repeats of death effector domain (DED) of caspase-8, but lacking the C-terminal half of the proteolytic domain. Reverse transcriptase (RT)-polymerase chain reaction (PCR) analysis revealed the dominant expression of caspase-8L transcript compared to the intact form of caspase-8 in human peripheral blood lymphocyte (PBL) and T cells. In patients with systemic lupus erythematosus (SLE), imbalanced expression of caspase-8L transcript was identified. These results suggest the important role of caspase-8L in the modulation of apoptosis.


L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:322611 CAPLUS
DOCUMENT NUMBER: 139:243521
TITLE: Bfl-1S, a novel alternative splice variant of Bfl-1, localizes in the nucleus via its C-terminus and prevents cell death
AUTHOR(S): Ko, Jae-Kyun; Lee, Min-Jung; Cho, Sun-Hee; Cho,

Jung-Ah; Lee, Bo-Young; Koh, Jason Soonju; Lee, Seung-Sook; Shim, Yhong-Hee; Kim, Chul-Woo
CORPORATE SOURCE: Tumor Immunity Medical Research Center and Cancer Research Institute, Department of Pathology, Seoul National University College of Medicine, Seoul, S. Korea
SOURCE: Oncogene (2003), 22(16), 2457-2465
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bfl-1 is an antiapoptotic Bcl-2 family member and a mouse A1 homolog. The mouse A1 has been reported to have three isoforms, but little is known about human Bfl-1. By reverse-transcriptase polymerase chain reaction anal., we have identified Bfl-1S (short form), an alternative splice variant of Bfl-1. The Bfl-1S primary sequence contains four conserved Bcl-2 homol. (BH) domains and a pos.-charged C-terminus containing KKRK amino acids. The expression of Bfl-1S mRNA was detected predominantly in normal lymph nodes and in B-lymphoid leukemia cells. Confocal microscopic anal. using green fluorescence protein fusion proteins demonstrated that Bfl-1S is localized in the nucleus by its C-terminus as an intrinsic nuclear localization sequence. Bfl-1S acts as an antiapoptotic agent in coexpression expts. with Bax, a proapoptotic mol. The expression of Bfl-1S provided significant resistance against staurosporine (STS) treatments in Molt-4 human T-leukemia cells. Bfl-1S also significantly inhibited the cleavage of Bid, and of caspases 3 and 8 against STS treatment. These results indicate that Bfl-1S is a novel human Bcl-2 family member that possesses antiapoptotic function.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:505403 CAPLUS
DOCUMENT NUMBER: 137:83614
TITLE: Regulating apoptosis by modulating splice variants of Tid1
INVENTOR(S): Syken, Joshua; Munger, Karl
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: U.S. Pat. Appl. Publ., 64 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 20020086844 | A1 | 20020704 | US 2001-908992 | 20010719 <-- |
| US 6825005 | B2 | 20041130 | | |
| PRIORITY APPLN. INFO.: | | | US 2000-219718P P | 20000719 |
| | | | US 2000-219537P P | 20000720 |

AB The invention provides isolated nucleic acids and vectors encoding two splice forms of Tid1 (Tid-1L and Tid-1S) and cells and non-human organisms comprising such. The invention further provides methods for modulating apoptosis in a cell by modulating the amount and/or activity of these two splice forms relative to each other. Such methods can be used in vivo and in vitro, e.g., in cell cultures, for either making cells more susceptible to apoptosis or more resistant to it.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:139958 CAPLUS
DOCUMENT NUMBER: 130:195769
TITLE: TRAIL-R3 and DR5 receptors and their splice variants, nucleic acids encoding the same, and methods of use
INVENTOR(S): Alnemri, Emad S.
PATENT ASSIGNEE(S): Idun Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9909165 | A1 | 19990225 | WO 1998-US16945 | 19980814 <-- |
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| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2301202 | A1 | 19990225 | CA 1998-2301202 | 19980814 <-- |
| AU 9887844 | A | 19990308 | AU 1998-87844 | 19980814 <-- |
| EP 1003864 | A1 | 20000531 | EP 1998-939413 | 19980814 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001514888 | T | 20010918 | JP 2000-509829 | 19980814 <-- |
| US 20010029030 | A1 | 20011011 | US 1998-134618 | 19980814 <-- |
| US 6417328 | B2 | 20020709 | | |
| US 20020115154 | A1 | 20020822 | US 2002-67615 | 20020204 <-- |
| US 20020161195 | A1 | 20021031 | US 2002-76754 | 20020212 <-- |
| US 20020161196 | A1 | 20021031 | US 2002-76773 | 20020212 <-- |

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|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1997-55906P | P | 19970815 |
| | US 1998-134618 | A3 | 19980814 |
| | WO 1998-US16945 | W | 19980814 |

AB In accordance with the present invention, there are provided isolated mammalian TRAIL receptor proteins, antibodies thereto, therapeutic compns., and nucleic acids encoding such. Novel human members of the TRAIL receptor protein family referred to as DR5 and TRAIL-R3 are provided that are capable of binding to the cytotoxic ligand TRAIL. Similarly, DR5s is a splice variant containing a truncated death domain, and thus also functions as an antagonistic decoy receptor. The polypeptides are cell-surface receptor proteins able to mediate apoptosis, and DR5 recruits caspase-8, caspase-10 and FLAME-1 to the death signaling pathway. Bioassays and therapeutic methods employing invention DR5 and TRAIL-R3 proteins are also provided.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 10:51:33 ON 11 NOV 2008
L1             0 S (WALLACH OR VARFOLOMEEV OR  PEWZNER-JUNG OR KANG OR MOSHE) AN
L2             3 S (CASPASE 8) (P) HEMATOPOIESIS AND PD<=20041026
L3             3 DUP REM L2 (0 DUPLICATES REMOVED)
L4            15 S (CASPASE 8) (S) (SPLICE VARIANT) AND PD<=20041026
L5             6 DUP REM L4 (9 DUPLICATES REMOVED)

=> S (CASPASE 8) (S) (SPLICE VARIANT)
L6            38 (CASPASE 8) (S) (SPLICE VARIANT)

=> Dup Rem L6
PROCESSING COMPLETED FOR L6
L7            18 DUP REM L6 (20 DUPLICATES REMOVED)
                 ANSWERS '1-7' FROM FILE MEDLINE
                 ANSWER '8' FROM FILE BIOSIS
                 ANSWERS '9-18' FROM FILE CAPLUS

=> S L7 and hematopoiesis
L8             0 L7 AND HEMATOPOIESIS

=> D TI L7 1-18

L7   ANSWER 1 OF 18     MEDLINE on STN                  DUPLICATE 1
TI   Cellular FLICE-like inhibitory protein (C-FLIP): a novel target for cancer
     therapy.

L7   ANSWER 2 OF 18     MEDLINE on STN                  DUPLICATE 2
TI   MADD/DENN splice variant of the IG20 gene is a
     negative regulator of caspase-8 activation. Knockdown
     enhances TRAIL-induced apoptosis of cancer cells.

L7   ANSWER 3 OF 18     MEDLINE on STN                  DUPLICATE 3
TI   A novel strategy for preventing human CD8+ cytotoxic T lymphocyte-mediated
     cytotoxicity against pig endothelial cells by overexpression of pig
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cellular FLICE-like inhibitory protein (c-FLIP) gene.

L7 ANSWER 4 OF 18 MEDLINE on STN DUPLICATE 4
TI Rapid turnover of c-FLIPshort is determined by its unique C-terminal tail.

L7 ANSWER 5 OF 18 MEDLINE on STN DUPLICATE 5
TI IG20 (MADD splice variant-5), a proapoptotic protein, interacts with DR4/DR5 and enhances TRAIL-induced apoptosis by increasing recruitment of FADD and caspase-8 to the DISC.

L7 ANSWER 6 OF 18 MEDLINE on STN DUPLICATE 6
TI Cellular FLICE-inhibitory protein splice variants inhibit different steps of caspase-8 activation at the CD95 death-inducing signaling complex.

L7 ANSWER 7 OF 18 MEDLINE on STN DUPLICATE 7
TI Dominant expression of a novel splice variant of caspase-8 in human peripheral blood lymphocytes.

L7 ANSWER 8 OF 18 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Expression of caspase-8L, a functional splice variant of caspase-8, is modulated in human T cells and B cells after activation by antigen receptor.

L7 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Up-regulation of c-FLIPshort by NFAT contributes to apoptosis resistance of short-term activated T cells

L7 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Cellular mechanisms of growth inhibition of human endometrial cancer cell line by an antagonist of growth hormone-releasing hormone

L7 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Role of IG20 Splice Variants in TRAIL Resistance

L7 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Selective inhibition of IG20 splice variants to treat cancers

L7 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Caspase 8L, a novel inhibitory isoform of caspase 8, is associated with undifferentiated neuroblastoma

L7 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Protein and cDNA sequences of human and mouse IG20 and DENN-SV splice variants and their therapeutic uses

L7 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Caspase-8L expression protects CD34+ hematopoietic progenitor cells and leukemic cells from CD95-mediated apoptosis

L7 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Bfl-1S, a novel alternative splice variant of Bfl-1, localizes in the nucleus via its C-terminus and prevents cell death

L7 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI Regulating apoptosis by modulating splice variants of Tid1

L7 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
TI TRAIL-R3 and DR5 receptors and their splice variants, nucleic acids encoding the same, and methods of use

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